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BENTLEY PHARM INC

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## OVERVIEW

Bentley Pharmaceuticals, Inc. is a drug delivery company specializing in the development and commercialization of products based upon innovative drug delivery systems. Although the Company is a domestic, publicly traded organization (BNT: AMEX), the vast majority of revenues are derived from Europe where the company manufactures and markets more than forty product presentations.

Our commercialized products are concentrated in four therapeutic categories of cardiovascular, gastrointestinal, anti-infective and CNS.

Bentley recently initiated a domestic strategy with the acquisition of proprietary permeation excipient technology and the establishment of a product development laboratory capable of creating and optimizing pharmaceutical formulations. Our technology consists of a series of chemicals, some of which, are GRAS (Generally Recognized As Safe) excipients that enhance the permeability of drugs administered through skin, across mucosa, through the cornea or the blood-brain barrier in a variety of independent pharmaceutical formats.

It is the format independence that sets this technology apart from other drug delivery technology. Studies have demonstrated that these excipients enhance the absorption of pharmaceutical products whether formulated in creams, ointments, gels, patches, solutions, lotions, or suppositories and effective with both hydrophilic and lipophilic agents.

We believe that in addition to the patent protection of products developed utilizing our technology, there is significant economic and scientific advantages associated with the GRAS status of these excipients, which allow for a more expedient and less-costly path to commercialization.

A Drug Master File (DMF) is established for reference with the US Food and Drug Administration.

Some of the potential applications are briefly summarized below:

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BENTLEY PHARM INC

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### TRANSDERMAL SUMMARY

*In vitro* experiments have demonstrated that our technology can enhance the transdermal permeation of a wide variety of drugs spanning an impressive range of molecular weights. Dynamic formulations (creams, ointments, gels, patches, or solutions) can be designed to target specific layers of the skin for regional and topical delivery, or designed to deliver a product for systemic absorption. These excipients have also proven to provide a homogeneous distribution and compatibility with patch adhesives. Various transdermal applications include:

- ◊ Hormone Replacement Therapy: estradiol, levonorgestrel, testosterone
- ◊ Antihypertensive agents: propranolol,
- ◊ Anti-anxiety agents: benzodiazepines
- ◊ NSAIDs: ketoprofen, diclofenac, ibuprofen, indomethacin, etc.
- ◊ Antifungals: clotrimazole, itraconazole, ketoconazole, miconazole, etc.
- ◊ Vasodilators & Erectile Dysfunction: PGE1, etc.
- ◊ Corticosteroids: hydrocortisone, fluticasone, triamcinolone, etc.
- ◊ Antivirals: acyclovir
- ◊ Anti-emetics: scopolamine
- ◊ Pain Management: fentanyl, hydromorphone, hydrocodone
- ◊ Anesthetics: etidocaine, lidocaine, xylocaine etc.
- ◊ Antibiotics: erythromycin, etc.
- ◊ Oncological: 5-fluorouracil, methotrexate

### DERMATOLOGICAL

*In vitro* and *in vivo* studies have demonstrated efficacy for enhancing various dermatological drugs including:

- ◊ Corticosteroids: hydrocortisone, fluticasone, etc.
- ◊ Anti-acne agents: retinoic acid, 13-cis-retinoic acid, erythromycin
- ◊ Skin cancer treatment agents: 5-fluorouracil
- ◊ Psoriasis: methotrexate, etc.

### OPHTHALMIC

Proven enhancement has been shown *in vitro* through corneal tissue with:

- ◊ timolol maleate
- ◊ indomethacin

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BENTLEY PHARM INC

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- ◇ demeclocycline (antiglaucoma drug) – 20% reduction in ocular pressure

#### INTRANASAL & MUCOSAL (PEPTIDES)

These excipients have also been combined successfully with large molecular weight products such as calcitonin and insulin to successfully facilitate nasal delivery and absorption. Tests have found these formulations are much more effective than any competitive product on the market.

Nasal application of insulin when combined with one of these excipients has a bioavailability of 40% as compared to the same drug dosage injected directly into the bloodstream. This is based on a yearlong preclinical study involving over 120 canine subjects. Other intranasal efficacy studies show extremely promising results for the delivery of other peptides including:

- ◇ Calcitonin
- ◇ Insulin
- ◇ Endorphins

#### ANTIFUNGAL

Results have indicated that *ketconazole* can be absorbed through the stratum corneum and retained in the viable skin layer. Similar results have been achieved with *itraconazole* and *clotrimazole*. These formulations provide a way to combat intractable fungal infections in the stratum corneum of the palms of the hands, the soles of the feet, or in the nail bed, occurring especially in immuno-compromised individuals such as AIDS patients.

#### ANTI-INFLAMMATORY/PSORIASIS

Anti-psoriatic drugs, such as methotrexate (MTX), both *in vitro* and *in vivo* have been previously investigated successfully. MTX has been used to treat severe psoriatic patients via oral administration, but this modality has associated serious side effects.

#### CNS AGENTS

Results have shown that anti-anxiety agents such as diazepam can be effectively enhanced through the skin using the permeation enhancement technology.

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BENTLEY PHARM INC

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### SAFETY STUDIES

Extensive safety studies have been performed and are outlined in our DMF. This is a summary:

- ◇ Acute oral toxicity: The acute oral LD<sub>50</sub> value in rats exceeded 5 g/kg.
- ◇ Acute dermal toxicity: The acute dermal LD<sub>50</sub> value in rabbits exceeded 5 g/kg.
- ◇ Irritation: No irritation was produced by the excipient applied full strength to intact or abraded rabbit skin for 24 hours under occlusion or to the backs of hairless mice or swine. Tested at 10% in petrolatum, the excipient produced no irritation after a 48-hour closed-patch test on human volunteers.
- ◇ Sensitization: A maximization test was carried out on 25 human volunteers. The material was tested at a concentration of 10% in petrolatum and produced no sensitization reactions.
- ◇ Mutagenicity: no mutagenic effects
- ◇ Skin Staining: none
- ◇ Phototoxicity: No phototoxic effects were reported for the excipient.
- ◇ Intranasal Irritation: A 28-day acute intranasal toxicity study in rats revealed no unexpected alterations in hematology or serum chemistry values associated with the administration of the permeation excipient; also, no irritation nor systemic toxicity, meticulous examination revealed no gross differences between the treated site (nostril and passage) and the untreated side in rats dosed with the excipient, vehicle or excipient.
- ◇ Human exposure: The safety of the excipients has been well-characterized since the human population has been exposed to much higher concentrations of these substances in amounts far greater than those required for permeation enhancement.

### FORMULATIONS AND STABILITY

Compatibility has been demonstrated in many drug platforms, including patches, creams, lotions, gels, solutions, etc. Impressive permeation enhancement activity has been demonstrated at very low amounts of our excipients. Formulations containing varying amounts of enhancers have shown excellent stability for up to 48 months. Moreover, the pleasant fragrance is a great advantage when compared with other available enhancers, which have objectionable odors.

### SAMPLE DATA

Sample data has been attached to illustrate the various formulations that document the capabilities and advantages of applying this technology.

•Estradiol                      •Testosterone                      •Clotrimazole                      •Diclofenac  
•Calcitonin

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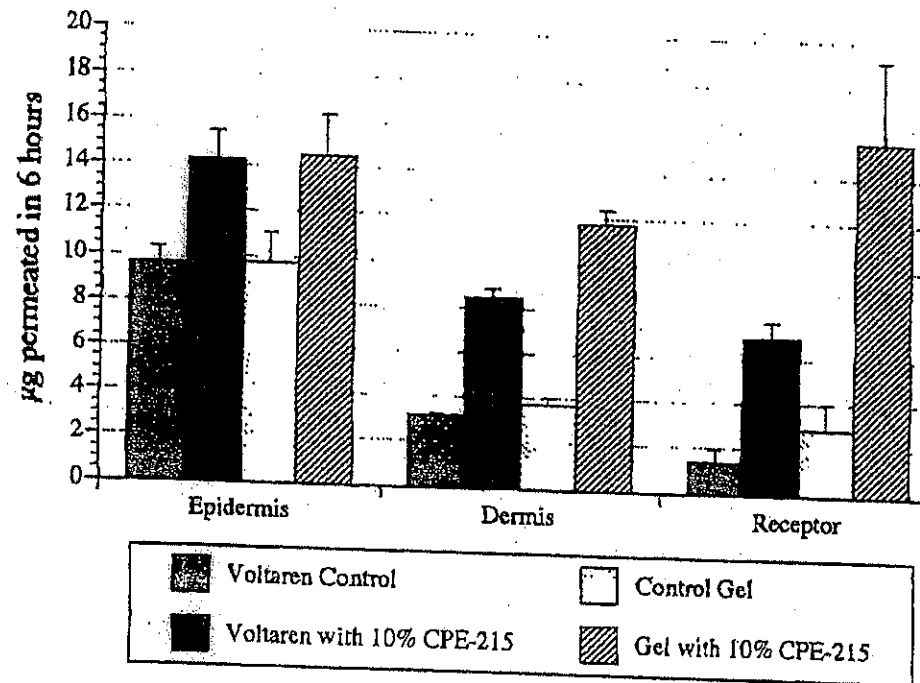
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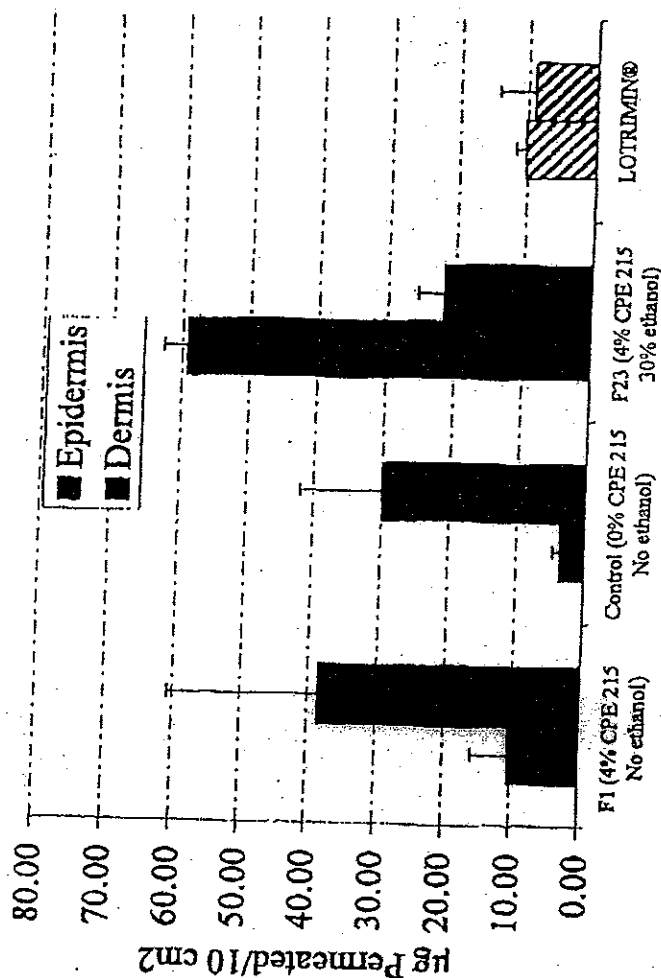
BENTLEY PHARM INC

CHOCOTRON

**Flux of Diclofenac through CD hairless rat skin**  
 1% Gels; 50 mg/0.636 cm<sup>2</sup> dose-Static cells experiment



# Clotrimazole Levels In Vivo



7 Hour Permeation Study; Guinea Pig

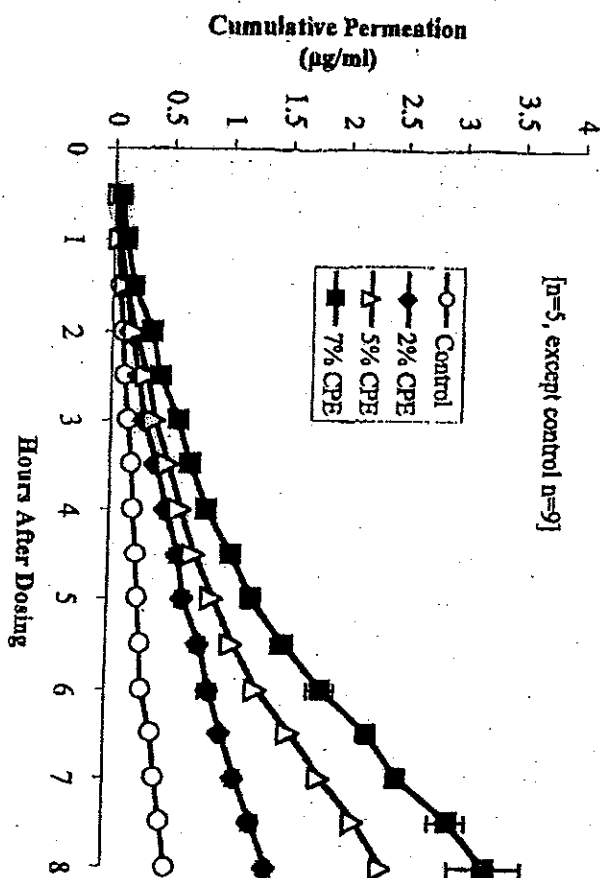
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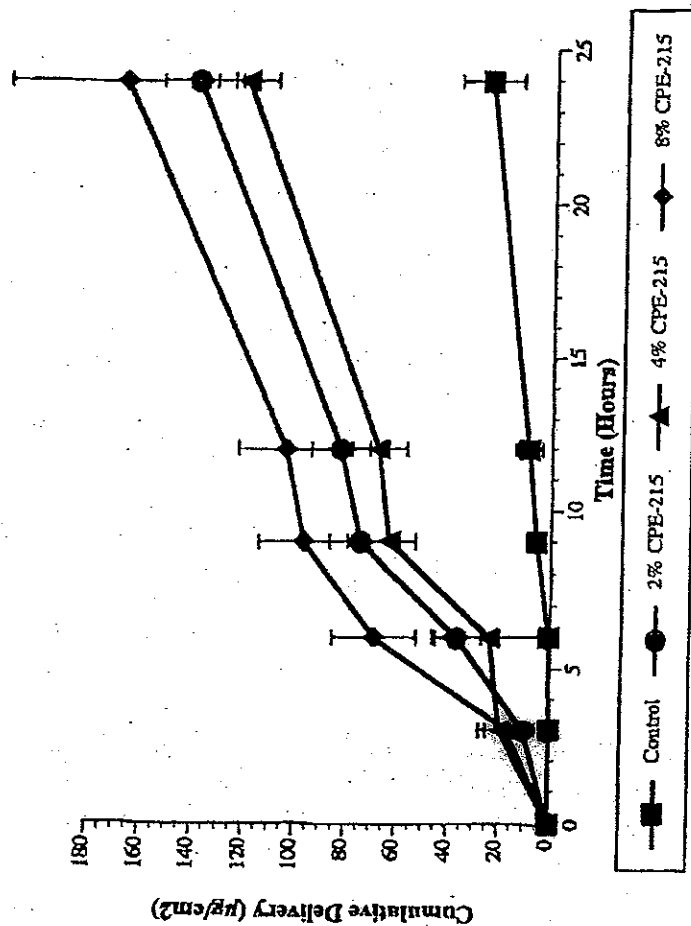
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# *In Vitro* Permeation of Timolol Through Perfused Rabbit Cornea



Testosterone Skin Permeation Enhancement with CPE-215  
Franz Cells: n=6 hairless rat skin







Laboratorios Belmac, S.A.

RECIBIDO 15 JUN. 1999



ETHYPHARM  
Marqués de la Ensenada, 16  
28004 MADRID

Att.: Mr. Adolfo de Basilio  
General Manager

Madrid, June 11<sup>th</sup>, 1999

Dear Sir,

Due to the last conversations held about various matters of mutual interest, I should like to confirm you that the company policies about commercial promotion that BELMAC has been carrying out from some time ago by the ways of communication and advertising, in particular, about our product BELMAZOL, always have been guided by the principle of honesty referent to the content of the promotional message, that is, the specific, differentiated and most significant contribution that the Product may offer to consumer sectorial market of pharmaceutical products in the aggregate supply of all Companies according to the procedures and discipline that the market itself and the health authorities require.

In this respect, we want to inform and guarantee you at the same time, the intent of BELMAC on respecting the above mentioned norms of advertising and the discipline of economic laws of market which govern the commercial relations in our country.

Finally, let me stress to you that, in no case and under any circumstances in the past, by commercial pressure, growing competition, public opinion or other, we have ever intended to harm the interests of ETHYPHARM, with which it does exists from many years a business relationship that we consider at the same time fully satisfactory, and, as far as we know, it remains safe and undisturbed up to now.

We would like, based on the foregoing, to convey to you our utmost sincere desire and willingness of keeping the spirit of trust, understanding, and collaboration, that ever has prevailed between both Companies.

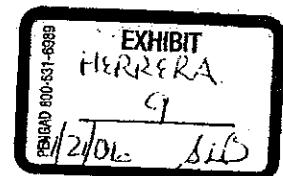
Should for any reason the content and the meaning of our sentiments at this moment not deem as clear as we have wished to express in this document, I invite you for a meeting to address or clarify any issue that you may consider appropriate.

Yours sincerely,

Adolfo Herrera  
General Manager

**BELMAC**

Monleagón, 9 - 1.ª planta - 28033 MADRID - Tel.: 91 388 72 01 - Fax: 91 388 76 47  
Fábrica: Polígono Málpica, s/n, 4. 50016 ZARAGOZA - Tel.: 976 57 17 84 - Fax: 976 57 26 63



EP 002436

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ethypharm

**Ethypharm**  
Drug Delivery Solutions

Madrid, 26 de Enero del 2000

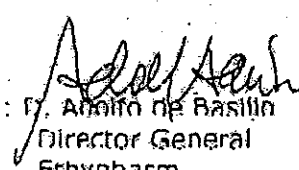
Adjunto los precios de fabricación y suministro para el año 2000, para su aceptación.

### Precios de Belmac para Ethypharm

- Encapsulado ..... 300 ptas/1000 dosis
- Exportación ..... 300 ptas/1000 dosis
- Costo fijo de fabricación (incluye dos turnos) ..... 2.666.666 ptas  
Este precio es para doce meses.
- Costo variable de fabricación por producto:
  - Omeprazol ..... 500.000 ptas/1.250.000 dosis
  - Piroxicam ..... 400.000 ptas/2.000.000 dosis
  - Vincamina ..... 400.000 ptas/1.000.000 dosis
  - Aspirina ..... 200.000 ptas/1.700.000 dosis
  - Indometacina ..... 400.000 ptas/1.500.000 dosis
  - Lansoprazol ..... 400.000 ptas/850.000 dosis
- Puesta en frasco todo incluido excepto pellets ..... 90 ptas
- Trabajo fin de semana a doble turno ..... 312.500 ptas
- Aumento coste fijo cuando incluyamos la nueva máquina 1.250.000 ptas.

### Precios de Ethypharm para Belmac

- Suministro de microgránulos de Omeprazol ..... 33.500 ptas.  
(incluyendo el principio activo y para una riqueza de 85.5 mg/g)  
Este precio está comprendido para un precio de compra del ingrediente activo de 1.000 dólares.

Fdo.:   
F. Adolfo de Basilio  
Director General  
Ethypharm

Fdo.:   
D. Adolfo Herrera  
Director General  
Belmac

Marqués de la Ensenada 4 - Centro Colon - 28004 Madrid (España)  
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Correo: ethypharm@ethypharm.es - Pág. Web: http://www.ethypharm.com

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IBERFORO

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**ethypharm****Ethypharm**  
Drug Delivery Solutions

Madrid, 26 janvier 2000

Ci-joint les prix de fabrication et de livraison pour l'an 2000, pour leur acceptation.

**Prix de Belmac pour Ethypharm**

- Encapsulation ..... 300 ptas/1000 doses
- Exportation ..... 300 ptas/1000 doses
- Coût fixe de fabrication (deux équipes incluses) ..... 2.666.666 ptas  
Ce prix est valable pour douze mois.
- Coût variable de fabrication par produit:
  - Oméprazole ..... 500.000 ptas/1.250.000 doses
  - Piroxicam ..... 400.000 ptas/2.000.000 doses
  - Vincamine ..... 400.000 ptas/1.000.000 doses
  - Aspirine ..... 200.000 ptas/1.700.000 doses
  - Indométacine ..... 400.000 ptas/1.500.000 doses
  - Lansoprazole ..... 400.000 ptas/850.000 doses
- Mise en flacon tout inclus excepté les pellets ..... 90 ptas.
- Travail week end avec deux équipes à tour de rôle ..... 312.500 ptas.
- Augmentation coût fixe quand sera incluse la nouvelle machine 1.250.000 ptas.

**Prix d'Ethypharm pour Belmac**

- Livraison de microgranules d'Oméprazole ..... 33.500 ptas.  
(Principe actif inclus et pour une richesse de 85.5 mg/g)  
Ce prix est compris pour un prix d'achat de l'ingrédient actif de 1.000 dollars.

**Signé:** M. Adolfo de Basilio  
Directeur Général  
Ethypharm

**Signé:** M. Adolfo Herrera  
Directeur Général  
Belmac

Marqués de la Encarnada, 18 - Centro Cádiz - 28004 Madrid (España)  
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[logo] **ethypharm**

[logo] **ethypharm**  
Drug Delivery Solutions

Madrid, January 26, 2000

I attach prices for manufacture and supply for the year 2000, for your approval.

**Prices from Belmac to Ethypharm**

* Encapsulation	300 ptas/ 1000 doses
* Export	300 ptas/ 1000 doses
* Fixed cost of manufacture (includes two shifts) this price is for 12 months	2,666,666 ptas
* Variable cost of manufacture per product:	
- Omeprazole	500,000 ptas/ 1,250,000 doses
- Piroxicam	400,000 ptas/ 2,000,000 doses
- Vincamine	400,000 ptas/ 1,000,000 doses
- Aspirin	200,000 ptas/ 1,700,000 doses
- Indomethacin	400,000 ptas/ 1,500,000 doses
- Lansoprazole	400,000 ptas/ 850,000 doses
* Packaging in glass all inclusive except pellets	90 ptas
* Weekend work double shifts	312,500 ptas
* Increase in fixed costs when we include new machine	1,250,000 ptas

**Prices from Ethypharm to Belmac**

* Supply of Omeprazole microgranules (including active ingredient at a concentration of 85.5 mg/g)	33,500 ptas
This price is for a purchase price of active ingredient of 1,000 dollars.	

[signature]  
Signed: Adolfo Basilio  
General director  
Ethypharm

[signature]  
Signed: Adolfo Herrera  
General Director  
Belmac

## LABORATORIOS BELMAC, S.A.

HOJA DE ENVÍO DE FAX	
PARA: D. Ignacio Alvarez	DE: Adolfo Herrera
ORGANIZACIÓN: Ethypharm	FECHA: 31 de Octubre de 2.000
NÚMERO DE FAX: 91 319 9159	Nº TOTAL DE PÁGINAS, PORTADA INCLUIDA: 2
NÚMERO DE TELÉFONO: 91 3085681	Nº DE REFERENCIA DEL REMITENTE:
ASUNTO:	SU Nº DE REFERENCIA:
<input type="checkbox"/> URGENTE <input type="checkbox"/> PARA REVISAR <input type="checkbox"/> COMENTARIOS <input type="checkbox"/> RESPONDA <input type="checkbox"/> RECICLAR	

Estimado Ignacio :

Tal como me habias solicitado, adjunto te remito copia del organigrama de nuestra Cía.

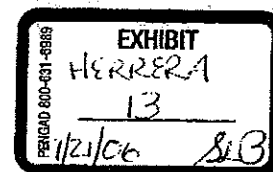
Recibe un cordial saludo.

  
 Fdº: Adolfo Herrera  
 Director General

*Enviado por mensaje  
 31/10/00*

LABORATORIOS BELMAC, S.A.  
 Montearagón, 9 - 28033 MADRID  
 Tfno.: 913887201 - Fax 913887647

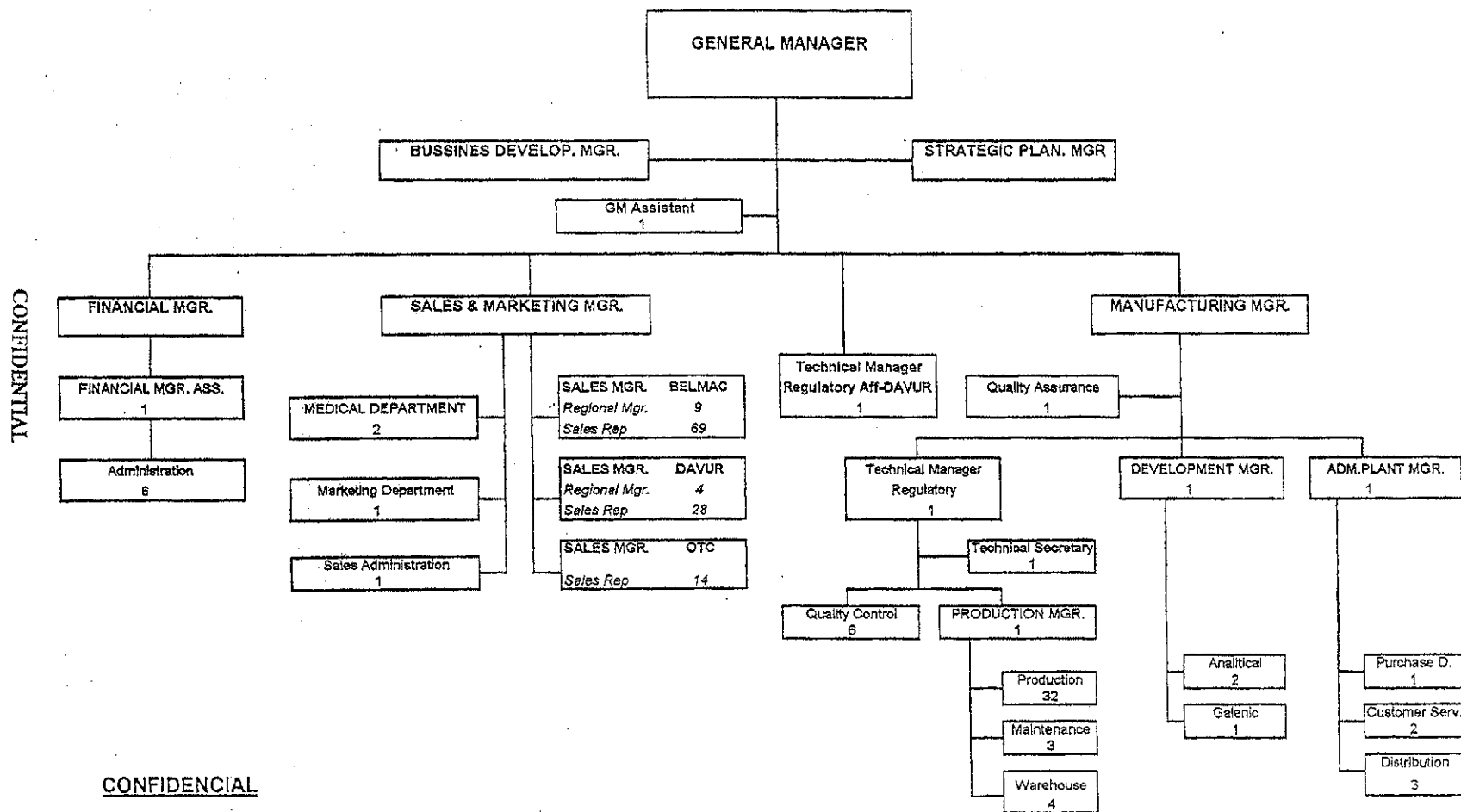
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BEL001051

A-426

## ORGANIZATION CHART



BEL001052

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**BELMAC LABORATORIES**

Fax Cover Sheet

To:  
D. Ignacio Alvarez

From:  
Adolfo Herrera

Company:  
Ethypharm

Date:  
October 31, 2000

Fax Number:  
91 319 9159

Total No. Pages, Incl. Cover Sheet:  
2

Telephone Number:  
913085681

Sender Reference No.:

Subject:

Reference No.:

Urgent

For Review

Comments

Respond

Recycle

Dear Ignacio:

As you had requested, I am attaching a copy of the organizational chart of our company.

I send a cordial greeting.

[Signature]  
Adolfo Herrera  
General Director

BELMAC LABORATORIES  
Montearagón, 9 – 28033 MADRID  
Tel.: 913887201 – Fax 913887647

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BEL001051

Rough Translation for use by Attorneys During Depositions  
May not be Submitted to Court without Permission of Edwards Angell Palmer & Dodge, LLP

A-428



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 E-Mail : ethypharm@ethypharm.es

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 28004 Madrid - Spain

<http://www.ethypharm.com>

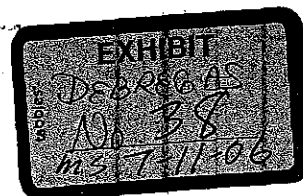
Fax no: 00 33 1 41 12 17 97	Page(s): 2	Date: 11/1/01
A/To: M. Eric Cailleret	From : D. Ignacio Álvarez de la Gala	
Cia/Company: Ethypharm S.A.	Dpt:	
Cc:	Cc: D. Adolfo de Basilio	
Subject :		

Cher M. Cailleret,

Veillez trouver ci-joint l' accord de prix signé avec Belmac pour l'année 2001.

Veillez agréer mes sincères salutations,

Fdo.: D. Ignacio Álvarez de la Gala



If you have received this communication in error, please notify us by telephone and consider that any dissemination, distribution or copy of this fax is strictly prohibited

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 EP 002917

A-429





Madrid, 20 de Diciembre de 2000


**PRECIOS DE FABRICACION Y SUMINISTRO PARA EL AÑO 2001**

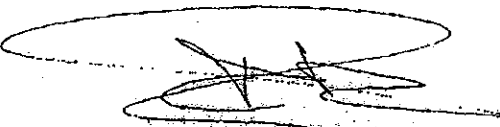
**Precios de Belmac para Ethypharm**

- Encapsulado..... 600 ptas/ 1000 dosis
- Exportación..... 300 ptas/ 1000 dosis
- Costo fijo de fabricación (incluye dos turnos dos GS)..... 4.073.333ptas / 17.500
- Este precio es para doce meses.
- Costo variable de fabricación por producto:
  - Omeprazol ..... 520.000 ptas/ 1.250.000 dosis
  - Piroxicam ..... 416.000 ptas/ 2.000.000 dosis
  - Vincamina ..... 416.000 ptas/ 1.000.000 dosis
  - Aspirina ..... 208.000 ptas/ 1.700.000 dosis
  - Indometacina ..... 416.000 ptas/ 1.500.000 dosis
  - Lansoprazol ..... 416.000 ptas/ 850.000 dosis
- Puesta en frasco todo incluido excepto pellets ..... 100 ptas
- Trabajo fin de semana a doble turno ..... 325.000 ptas

**Precios de Ethypharm para Belmac**

- Suministro de microgránulos de Omeprazol ..... 29.500 ptas / kg  
(Incluyendo el principio activo y para una riqueza de 85.5 mg/g)
- Estos precios podrán ser modificados de mutuo acuerdo trimestralmente.

  
Fdo: D. Adolfo de Basilio  
Director General  
Ethypharm

  
Fdo: D. Adolfo Herrera  
Director General  
Belmac

Marqués de la Enchada, 16 - Centro Códex - 28004 Madrid (España)  
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Correo-e: ethypharm@ethypharm.es - Pág. Web: http://www.ethypharm.com

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EP 002918

A-430

## Ethypharm

Drug Delivery Solutions

Madrid, December 20, 2000

Belmac's prices for Ethypharm

- |  |                                   |
|--|-----------------------------------|
| - Drug capsule   | 600 pesetas / 1,000 doses         |
| - Exportation  | 300 pesetas / 1,000 doses         |
| - Fixed manufacturing cost (including two shifts two GS) | 4,073,333 pesetas                 |
| This price covers twelve months.                         |                                   |
| - Variable manufacturing cost per product:               |                                   |
| - Omeprazole   | 520,000 pesetas / 1,250,000 doses |
| - Piroxicam  | 416,000 pesetas / 2,000,000 doses |
| - Vincamina  | 416,000 pesetas / 1,000,000 doses |
| - Aspirin  | 208,000 pesetas / 1,700,000 doses |
| - Indometacina   | 416,000 pesetas / 1,500,000 doses |
| - Lansoprazole   | 416,000 pesetas / 850,000 doses   |
| - Drug Bottles all included except pellets               | 100 pesetas                       |
| - Work during weekend, double shift                      | 325,000 pesetas                   |

Ethypharm's prices for Belmac

- |  |                   |
|--|-------------------|
| - Omeprazole Microgranules supply                                  | 29,500 pesetas/kg |
| (Including the active ingredient and rated at 85.5mg/g)            |                   |
| This price may be modified by mutual agreement every three months. |                   |

[There follows an illegible signature].  
Signed: Adolfo de Basilio  
General Director, Ethypharm

[There follows an illegible signature].  
Signed: Adolfo Herrera  
General Director, Belmac

Marqués de la Ensenada, 16 – Centro Colón – 28004 Madrid (Spain)  
Tel.: +34 913 085 681 – Fax: +34 913 190 159  
E-mail: [ethypharm@ethypharm.es](mailto:ethypharm@ethypharm.es) – Web site: <http://www.ethypharm.com>

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EP 002918



Madrid, 26 de Enero del 2000

Adjunto los precios de fabricación y suministro para el año 2000, para su aceptación.

#### Precios de Belmac para Ethypharm

- Encapsulado ..... 300 ptas/1000 dosis
- Exportación ..... 300 ptas/1000 dosis
- Costo fijo de fabricación (incluye dos turnos) ..... 2.666.666 ptas  
Este precio es para doce meses.
- Costo variable de fabricación por producto:
  - Omeprazol ..... 500.000 ptas/1.250.000 dosis
  - Piroxicam ..... 400.000 ptas/2.000.000 dosis
  - Vincamina ..... 400.000 ptas/1.000.000 dosis
  - Aspirina ..... 200.000 ptas/1.700.000 dosis
  - Indometacina ..... 400.000 ptas/1.500.000 dosis
  - Lansoprazol ..... 400.000 ptas/850.000 dosis
- Puesta en frasco todo incluido excepto pellets ..... 90 ptas
- Trabajo fin de semana a doble turno ..... 312.500 ptas
- Aumento coste fijo cuando incluyamos la nueva máquina 1.250.000 ptas.

#### Precios de Ethypharm para Belmac

- Suministro de microgránulos de Omeprazol ..... 33.500 ptas.  
(incluyendo el principio activo y para una riqueza de 85.5 mg/g)  
Este precio está comprendido para un precio de compra del ingrediente activo de 1.000 dólares.

Fdo.: D. Adolfo de Basilio  
Director General  
Ethypharm

Fdo.: D. Adolfo Herrera  
Director-General  
Belmac

Marqués de la Ensenada, 16 - Centro Colón - 28004 Madrid (España)  
TEL.: +34 913 085 681 - FAX.: +34 913 199 159  
Correo-e: ethypharm@ethypharm.es - Pag. Web: http://www.ethypharm.com

CONFIDENTIAL  
EP 002922

A-431

## **ETHYPHARM**

Drug Delivery Solutions

Madrid, January 26, 2000

Attached are the manufacturing and supply prices for the year 2000, for your acceptance.

### **Belmac's prices for Ethypharm**

- Drug capsule 300 pesetas / 1,000 doses
- Exportation 300 pesetas / 1,000 doses
- Fixed manufacturing cost (including two shifts) 2,666,666 pesetas  
This price covers twelve months.
- Variable manufacturing cost per product:
  - Omeprazole 500,000 pesetas / 1,250,000 doses
  - Piroxicam 400,000 pesetas / 2,000,000 doses
  - Vincamina 400,000 pesetas / 1,000,000 doses
  - Aspirin 200,000 pesetas / 1,700,000 doses
  - Indometacina 400,000 pesetas / 1,500,000 doses
  - Lansoprazole 400,000 pesetas / 850,000 doses
- Drug Bottles all included except pellets 90 pesetas
- Work during weekend, double shift 312,500 pesetas
- A fixed cost will be added when the new machinery is included 1,250,000 pesetas

### **Ethypharm's prices for Belmac**

- Omeprazole Microgranules supply 33,500 pesetas  
(including the active ingredient and rated at 85.5mg/g)

This price is understood with a purchasing price of the active ingredient of 1,000 dollars.

[There follows an illegible signature].

[There follows an illegible signature].

Signed: Adolfo de Basilio  
General Director, Ethypharm

Signed: Adolfo Herrera  
General Director, Belmac

Marqués de la Ensenada, 16 – Centro Colón – 28004 Madrid (Spain)  
Tel.: +34 913 085 681 – Fax: +34 913 190 159  
E-mail: [ethypharm@ethypharm.es](mailto:ethypharm@ethypharm.es) – Web site: <http://www.ethypharm.com>

CONFIDENTIAL

EP 002918



Madrid, 26 janvier 2000

Ci-joint les prix de fabrication et de livraison pour l'an 2000, pour leur acceptation.

#### Prix de Belmac pour Ethypharm

- Encapsulation ..... 300 ptas/1000 doses
- Exportation ..... 300 ptas/1000 doses
- Coût fixe de fabrication (deux équipes incluses) ..... 2.666.666 ptas  
Ce prix est valable pour douze mois.
- Coût variable de fabrication par produit:
  - Oméprazole ..... 500.000 ptas/1.250.000 doses
  - Piroxicam ..... 400.000 ptas/2.000.000 doses
  - Vincamine ..... 400.000 ptas/1.000.000 doses
  - Aspirine ..... 200.000 ptas/1.700.000 doses
  - Indométacine ..... 400.000 ptas/1.500.000 doses
  - Lansoprazole ..... 400.000 ptas/850.000 doses
- Mise en flacon tout inclut excepté les pellets ..... 90 ptas.
- Travail week end avec deux équipes à tour de rôle ..... 312.500 ptas.
- Augmentation coût fixe quand sera incluse la nouvelle machine 1.250.000 ptas.

#### Prix d'Ethypharm pour Belmac

- Livraison de microgranules d'Oméprazole ..... 33.500 ptas.  
(Principe actif inclut et pour une richesse de 85.5 mg/g)  
Ce prix est compris pour un prix d'achat de l'ingrédient actif de 1.000 dollars.

Signé: M. Adolfo de Basilio  
Directeur Général  
Ethypharm

Signé: M. Adolfo Herrera  
Directeur Général  
Belmac

Marqués de la Ensenada, 16 - Centro Colón - 28004 Madrid (España)  
TEL: +34 913 085 681 - FAX: +34 913 199 159  
Correo-e: ethypharm@ethypharm.es - Pag. Web: <http://www.ethypharm.com>

CONFIDENTIAL  
EP 002923

A-432

Dear Mr. Cailleret,

Please find attached the price agreement signed with Belmac for the year 2001.

Best regards,

illegible initials

Signed: Ignacio Álvarez de la Gala

EP002917



Laboratoires PHARMALLIANCE  
63, rue Boudjema Moghni  
Hussein - Dey Alger  
Tel : (021) 23 34 06 / 23 35 42  
Fax : (021) 23 19 18

Mr A. HERRERA  
Laboratorios BELMAC  
28700 San Sebastian de Los Reyes  
Madrid  
Spain

Algiers, 06 December 2001

Dear Mr. Herrera;

Please find here enclosed the Confidentiality Agreement, duly signed by Mrs Amal Lamari,  
of the following products :

- Omeprazole 10 & 20 mg
- Enalapril 5 & 20 mg
- Simvastatine 20 mg

Could you please send us as soon as possible the corresponding files.

Thank you for your co- operation & Best regards.

A handwritten signature in dark ink, appearing to read "Ilhem Chafia GADRI".

Ilhem Chafia GADRI  
Affaires Réglementaires

Laboratoires Pharmalliance 63, rue Boudjema Moghni - Hussein-Dey - Alger  
Téléphone : (02) 23 34 06 / 23 35 42 Fax : (02) 23 19 18



BEL000496

A-434

**SUPPLY, MARKETING & DISTRIBUTION AGREEMENT**

**BETWEEN:**

**PHARMALLIANCE**, with head office in 63, Rue Boudjema Moghni Hussein-Dey, Alger-Algerie, represented by Amal Lamary Chairman, (Hereinafter called "PHARMALLIANCE");

**AND**

**LABORATORIOS BELMAC, S.A.**, with head office at San Sebastian de los Reyes, MADRID 28700, C/ Teide 4, Poligono Empresarial La Marina, represented by Mr. Adolfo Herrera Málaga, General Manager, holding powers for this deed, (Hereinafter called "BELMAC")

The parties have agreed and taken into written form, this commercial marketing and distribution agreement:

**FIRST**

PHARMALLIANCE agrees to buy from BELMAC the medicine "OMEPRazole" 20 mg and OMEPRazole 10mg capsules, according to the schedule and supplying plan, which will be agreed between the parties.

**SECOND**

BELMAC agrees to sell to PHARMALLIANCE the medicine "OMEPRazole" 20 mg and OMEPRazole 10mg capsules, at competitive prices, re-calculated every year

**THIRD**

The products supplied and sold to PHARMALLIANCE by BELMAC as the sole and exclusive manufacturer must be delivered C&F from the production plant in Zaragoza, Spain, to PHARMALLIANCE warehouse at ALGEL, ALGERIE, conditioned, packed in bulk and labelled according to the instructions, which PHARMALLIANCE will inform BELMAC about.

**FOURTH**

The price of each supply will have to be paid within 120 days from the AWB date.

**TENTH**

Neither Party shall be entitled to any compensation or indemnity as result of the termination of the agreement.

**CONFIDENTIAL**

**BEL000497**

**A-435**



**ELEVENTH**

In order to guarantee the success of the product omeprazol (PROTON), Belmac will assume part of the marketing and distribution costs of the product during the time that Belmac supply the product in Bottle labeled.

For each bottle of the product supplied by Belmac, Pharmalliance will emit an invoice to Belmac with the following charges:

Omeprazole 20mg in Bottle of 14 capsules	1,706 Euros.
Omeprazole 20mg in Bottle of 28 capsules	3,265 Euros.
Omeprazole 10mg in Bottle of 28 capsules	1,874 Euros.

Payment will be made 120 days from AWB

**TWELVETH**

**Supply Prices C&F Alger (Algerie)**

Omeprazole 20mg in Bottle of 14 capsules	3,20 Euros.
Omeprazole 20mg in Bottle of 28 capsules	6,13 Euros.
Omeprazole 10mg in Bottle of 28 capsules	3,52 Euros.

This Confidentiality and Non -Disclosure covenant will survive and last for five (5) years after the termination of the Agreement.

This agreement was written in duplicate.

Alger, Algerie February

PHARMALLIANCE  
Amal Lamary

LABORATORIOS BELMAC, S.A.  
Adolfo Herrera

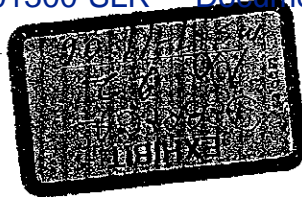
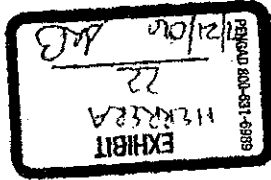
**CONFIDENTIAL**

**BEL000498**

**A-436**

A-437

EP 004846



Site de fabrication : L'Hermin de la Foudre - 8, P. 117 - 76121 Le Grand Chevalier Cedex - France - TEL : + 33 - 2 35 18 24 54 - FAX : + 33 - 2 35 18 24 51  
 Siège Social et fabrication : 21, rue Saint Martin - 76550 Hockley - France - TEL : + 33 - 1 30 88 12 20 - FAX : + 33 - 1 30 88 12 30  
 Direction Scientifique et Commerciale : 18, Rue de la Courbe - Bâtiment D - 92213 Saint-Cloud Cedex - France  
 TEL : + 33 - 1 41 12 17 20 - FAX : + 33 - 1 41 12 17 30 - Télécopieur : + 33 - 1 41 12 00 15 - Site Web : <http://www.ethypharm.com>  
 S.A. au capital de 6 000 000 € - RCS Nanterre B 311 959 813 - APE 242 C - Siret 311 959 813 00012

Yours sincerely,  
 Genard LEBLANC  
 General Manager

Patrice DEBERGAS  
 President

Dear sir,

We have received through Mr Adolfo de Basilio de Bastillo copy of your letter dated January 2, 2002 addressed to our subsidiary Ethypharm S.A. in Spain.

In order to further discuss the present situation, we reiterate our wish to have a meeting with your company prior to the effective termination of our agreements and propose to welcome you at our Saint Cloud offices during the week of February 18<sup>th</sup> 2002 and preferably Thursday 21<sup>st</sup> or Friday 22<sup>nd</sup> of February.

We thank you in advance for confirming your availability during that week and the date which is most convenient for you.

Looking forward to hearing from you,

For the attention of Mr DEBERGAS

Via Facsimile : 00 34 91 652 01 44  
 Confirmation by courier

Saint Cloud, February 1st, 2002

LABORATORIOS BELMAC S.A.  
 Telfa, 4 Planta Baja  
 Parque Empresarial "La Maritima"  
 28700 SAN SEBASTIAN DE LOS REYES  
 (Madrid)  
 SPAIN

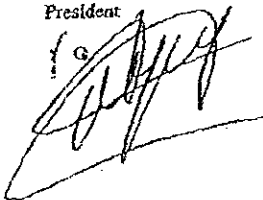


In order to further discuss the present situation, we reiterate our wish to have a meeting with your company prior to the effective termination of our agreements and propose to welcome you at our Saint Cloud offices during the week of February 18<sup>th</sup> 2002 and preferably Thursday 21<sup>st</sup> or Friday 22<sup>nd</sup> of February.

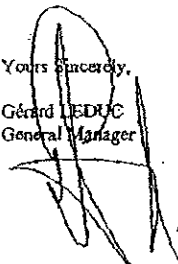
We thank you in advance for confirming your availability during that week and the date which is most convenient for you.

Looking forward to hearing from you,

Patrice DEBREGEAS  
President



Yours Sincerely,  
Gérard LEDUC  
General Manager



Direction Scientifique et Commerciale - 194, Bureau de la Colline - Bâtiment D - 92213 Saint-Cloud Cedex - France  
TEL : + 33 - 1 41 12 17 20 - FAX : + 33 - 1 41 12 17 30 - Valenciennes : + 33 - 1 41 12 00 76 - Site Web : <http://www.ethypharm.com>  
Siège Social et Fabrication : 21, rue Saint Martin - 78550 Houdan - France - TEL : + 33 - 1 30 88 17 20 - FAX : + 33 - 1 30 88 17 30  
Site de Fabrication : Chemin de la Poudrière - B.P. 117 - 78121 Le Grand Cheval Cedex - France - TEL : + 33 - 2 35 78 24 64 - FAX : + 33 - 2 35 78 24 61  
S.A. au capital de 6 000 000 F RCS Nanterre N° 315 000 031 - APE 24.49 C Siret 315 000 031 00012

E-4) PAS DE REponse  
E-2) OCCUPÉ  
E-1) RACCOURCI OU ERREUR LIGNE

CAUSE DE L'ERREUR  
E-3) RACCOURCI OU ERREUR LIGNE  
E-2) OCCUPÉ  
E-1) RACCOURCI OU ERREUR LIGNE

1031 TX MEMORISEE 00034916520144 OK 1/1  
PAGE RESULT  
TI ETHYPHARM SCL  
OPTION ADRESSE (GROUPE)

\* \* \* RAPPORT DE RESULTAT DE LA COMMUNICATION ( 1.FEV.2002.19:46 ) \* \* \*

P. 1

EP 004847

A-438

ETHYPHARM, S.A.  
194 Bureaux de la Colline  
Bâtiment D  
99213 Saint-Cloud Cedex  
France

Madrid, February 6<sup>th</sup>, 2.002

Att.: Mr. Patrice Debregeas  
Mr. Gérard Leduc

Dear Sirs,

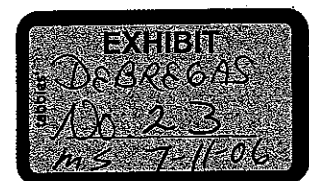
We have just received your letter dated February 1<sup>st</sup> 2.002, and in order to further discuss the present situation, we inform you that our intention is to have a meeting in your Saint Cloud offices next 21<sup>st</sup> February at 9,30am.

The people who will assist at the meeting will be Mr. Fernando Berenguer Zúñiga and I.

Looking forward to receiving your confirmation, we remain.

Sincerely yours.

Adolfo Herrera  
General Manager





LABORATORIOS BELMAC S.A.  
Teida, 4 Planta Baja  
Parque Empresarial "La Marina"  
28700 SAN SEBASTIAN DE LOS REYES  
(Madrid)  
SPAIN

Saint Cloud, February 11th, 2002

Via Facsimile : 00 34 91 652 01 44  
Confirmation by courier

For the attention of Mr HERRERA

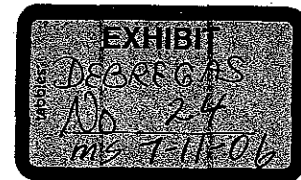
Dear sir,

Further to your letter of February 6<sup>th</sup>, 2002, we wish to confirm the meeting next February 21<sup>st</sup>, 2002 at our Saint Cloud offices at 9.30 a.m.

Looking forward to receiving you and Mr Berenguer Zuniga, we remain ,

Yours Sincerely,

Patrice DEBREGEAS  
President



Direction Scientifique et Commerciale : 194, Bureaux de la Colline - Bâtiment D - 92213 Saint-Cloud Cedex - France  
TEL. : + 33 - 1 41 12 17 20 - FAX : + 33 - 1 41 12 17 30 - Visioconférence : + 33 - 1 41 12 00 75 - Site Web : <http://www.ethypharm.com>  
Siège Social et Fabrication : 21, rue Saint Matthieu - 78550 Houdan - France - TEL. : + 33 - 1 30 88 17 20 - FAX + 33 - 1 30 88 17 30  
Site de Fabrication : Chemin de la Poudrière - B.P. 117 - 76121 Le Grand Quevilly Cedex - France - TEL + 33 - 2 35 18 24 64 - FAX + 33 - 2 35 18 24 61  
S.A. au capital de 6 000 000 F - RCS Versailles B 311 999 833 - APE 244 C - Siret 311 999 833 00032

EP 004845

A-440

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**From:** joannesse.roseline@ethypharm.com  
**Sent:** Thursday, March 21, 2002 7:09 PM  
**To:** herrera@belmac.com  
**Cc:** gérard.leduc@ethypharm.com; Debregeas.Patrice@ethypharm.com; ethypharm@ethypharm.es  
**Subject:** Agreement

**Importance:** High

**Attachments:** Belmac020321.doc; suministro02b.rtf



Belmac020321.docsuministro02b.rtf (34  
(20 KB) KB)

Dear Mr Herrera,

Please find attached anticipated copy by e-mail of Mr Leduc's letter and of your revised proposal.

Copy is also forwarded tonight by fax.

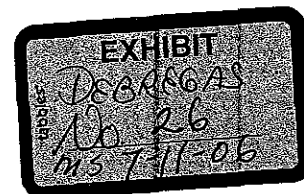
Looking forward to hearing from you,

Yours Sincerely, (See attached file:  
Belmac020321.doc) (See attached file: suministro02b.rtf)

Roseline JOANNESSE  
Directeur Juridique - groupe

ETHYPHARM S.A.  
194 Bureaux de la Colline  
Bat. D  
92213 Saint Cloud Cedex - France  
tel : 00 33 1 41 12 17 35  
fax : 00 33 1 41 12 17 30

1



CONFIDENTIAL  
EP 008591

A-441